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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/832,663	04/11/2001	Anthony J. Polak	LFS-5044	1850

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LIFESCAN/NUTTER MCCLENNEN & FISH LLP
155 SEAPORT BOULEVARD
BOSTON, MA 02210-2604

EXAMINER	
YANG, NELSON C	
ART UNIT	PAPER NUMBER
1641	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/832,663	POLAK ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,19,20,23-26,28-32,34-44,46 and 47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17,19,20,23-26,28-32,34-44,46 and 47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *11 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendment of claim 1 is acknowledged and has been entered.

2. Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

3. Claims 1-17, 19-20, 23-26, 28-32, 34-44, 46, 47 are currently under examination.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1-17, 19-20, 23-26, 29, 34-44, 46, 47 are rejected under 35 U.S.C. 103(a) as being anticipated by Schultz [US 6,256,522] in view of Krauth [US 4,954,435] and further in view of Vo-Dinh [US 5,864,397] and further in view of Mills et al. [US 6,123,700].

With respect to claim 1-4, 7-8, 19, 20, 23-26, 29, Schultz teaches a receptor material, Concanavalin A covalently attached to Rhodamine dye molecules, analog analyte comprising dextran covalently attached to fluorescein dye molecules located within a transparent capsule comprising a semi-permeable membrane comprising cellulose or polysulfone (column 10, lines 21-37, claim 1). Schultz further teaches a pH indicator located within the capsule (column 11, lines 1-5, claim 1), as well as a second dye of a second wavelength different from the first wavelength (column 13, lines 15-20). The rhodamine quenches emission fluorescence from the

fluorescein (column 10, lines 38-45). With respect to claim 4, the receptor material may be immobilized to a gel such as polyethylene glycol within the chamber (column 8, lines 11-27). Schultz fails to specifically teach using the pH indicator or a second dye as a reference dye, or that the binding substrate has a molecular imprint of the analyte, and also fails to teach that the device is seamless.

Krauth, however, teaches that in fluorescence assays, using a ratio of light signals, one signal being the reporter signal, and the other being the reference signal, provides a correction mechanism for obviating such variables such as fluctuation in the lamp output, variation in tube position, diameter, or optical quality (column 3, lines 50-61).

Vo-Dinh further teaches the use of a molecular imprint material designed to concentrate specific compounds of interest for improved sensitivity (column 6, lines 63-65).

Therefore it would have been obvious to one of ordinary skill in the art at the time of the invention to use the pH indicator as a reference dye as suggested by Krauth in the device of Schultz et al, in order to obviate such variables such as fluctuation in the lamp output, variation in tube position, diameter, or optical quality when detecting the presence of analytes. It would have further been obvious to use a molecular imprint material, as suggested by Vo-Dinh, in the device of Schultz, in order to concentrate specific compounds of interest for improved sensitivity.

Mills et al. further teach that a sealed, implantable, encapsulation device (column 4, lines 10-15), and further teach a technique of forming the device into one permanent seamless bulk material (column 18, lines 36-43), Mills et al. further provides motivation that this allows for long-term, cell-tight, seal integrity, without mechanically deforming the encapsulation device

surfaces (column 3, lines 50-67), while providing durability, compactness, easy maintainence, and economical to manufacture (column 4, lines 1-10).

Therefore, one of ordinary skill in the art at the time of the invention would have been motivated to make the invention of Schultz a seamless, unitary whole, as suggested by Mills et al., in order to provide long-term, cell-tight, seal integrity, without mechanically deforming the encapsulation device surfaces, while providing durability, compactness, easy maintainence, and economical to manufacture.

6. With respect to claims 5-6, although neither Schultz nor Krauth teaches a reference covalently bonded to the membrane or in the membrane, it would have been obvious to one having ordinary skill at the time was made to have the reference covalently bonded to the membrane or in the membrane, since it has been held that rearranging parts of an invention involves only routine skill in the art. *In re Japikse,* USPQ 70.

7. With respect to claims 9-12, Schultz teaches that the analyte and receptor may bind to form an analyte-receptor complex (column 6, lines 40-50) and comprise dextran (column 10, lines 20-37).

8. With respect to claims 13-17, Schultz teaches that the receptor material can be immobilized to a gel such as polyacrylamide (column 8, lines 20-28). Schultz further teaches that rhodamine dye molecules can be attached to the receptor material for quenching fluorescence (column 10, lines 25-45).

9. With respect to claims 34-36, Schultz teaches that the semi-permeable membrane comprising cellulose or polysulfone (column 10, lines 21-37, claim 1)

10. With respect to claim 37, Schultz teaches that the analyte-permeable membrane may also have a reflector comprising metallic particles immobilized on the surface of an ultrafiltration membrane (column 10, lines 1-10).

11. With respect to claims 38-39, Schultz teaches that the analyte being measured is glucose (column 10, line 25).

12. With respect to claims 40-43, while Schultz do not teach what the ratio of the empty space encapsulated by the capsule to a volume occupied by the binding substrate is, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranged involves only routine skill in the art. *In re Aller*, 105 USPQ 233. Furthermore, since applicant has not discussed any unexpected improvements or results using ratios between 0.05 and 5, between 0.5 and 3, or 1, it would have been obvious to a person of ordinary skill in the art to have used ratios between 0.05 and 5, between 0.5 and 3, or 1 through normal optimization techniques.

13. With respect to claims 44, 46, 47, the sensor unit may be placed underneath the skin (column 7, lines 27-36), illuminated with a laser (column 7, lines 38-45), and measuring absorption of light, including ultraviolet, visible or infrared (column 7, lines 15-25).

14. Claims 31-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz [US 6,256,522] in view of Krauth [US 4,954,435] and Vo-Dinh [US 5,864,397] and in view of Ketterl et al. [US 6,678,564], as applied to claim 1 above, and further in view of Ferri et al [Ferri et al, Direct eye visualization of Cfluorescence for immunocytochemistry and in situ hybridization, 2000, J Hist Cytochem, 48(3), 437-444]

The combination of Schultz, Vo-Dinh, Krauth and Ketterl et al. teach the use of a reference, as discussed above, but do not teach the use of cyanine dyes such as Cy5.

Ferri et al, however, teach that Cy5 provides a distinct fluorescent signal that can easily be separated from that of many other fluorochromes (p.437, col.1). Ferri et al further teach that a distinct advantage of Cy5 is the low autofluorescence found in many cells and tissues in the above wavelength range (p.437, col.1).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to use Cy5 as a reference in the device of Schultz, Krauth et al., Vo-Dinh, and Ketterl et al. as suggested by Ferri et al, as one would have been motivated to provide a distinct fluorescent signal that can be easily separated from other fluorochromes by using Cy5 as a reference.

15. Claim 28 is rejected under 35 U.S.C. 103(a) as being unpatentable over Schultz [US 6,256,522] in view of Krauth [US 4,954,435] and Vo-Dinh [US 5,864,397] and in view of Ketterl et al. [US 6,678,564], as applied to claim 1 above, and further in view of Bruchez et al [US 6,274,323].

Schultz, Vo-Dinh, Krauth, and Ketterl et al. teach the use of a reference, as discussed above, but fail to teach the use of quantum dots as a reference.

Bruchez et al., however, teach that semiconductor nanocrystals may be used to detect or track a single target, and can be used to in a variety of assays where other, less reliable, labeling methods have typically been used, including fluorescence microscopy, histology, cytology pathology, flow cytometry, FISH, signal amplification assays, DNA and protein sequencing,

immunoassays, immunohistochemical analysis, homogeneous assays, high throughput screening, and the like (column 16, lines 58-67).

Therefore it would have been obvious to use semiconductor nanocrystals, or quantum dots, instead of a label as a reference in the device of Schultz, Krauth, Vo-Dinh, and Ketterl et al. as suggested by Bruchez et al., in order to provide a more reliable labeling method.

Response to Arguments

16. Applicant's arguments with respect to claims 1-17, 19-20, 23-26, 28-32, 34-44, 46, 47 have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

17. No claims are allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571) 272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571)272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

20. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nelson Yang
Patent Examiner
Art Unit 1641

LONG V. LE 03/16/07
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600